

IN THE CLAIMS:

Please add the following claims:

--93. A device for amplifying a preselected polynucleotide in a sample by conducting a polynucleotide amplification reaction, the device comprising:

a solid substrate which is microfabricated to define:

a sample inlet port;

a flow system for micro- to picoliter volumes, comprising:

a sample flow channel extending from said inlet port; and

a polynucleotide amplification reaction chamber in fluid communication with said flow channel;

said chamber and said channel being of dissimilar dimension; and

a fluid exit port in fluid communication with said flow system; and

means for thermally cycling the contents of said chamber whereby in each cycle the temperature is controlled to dehybridize double stranded polynucleotide and to permit the in-vitro amplification of a preselected polynucleotide.

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94. The device of claim 93, wherein said amplification reaction is a polymerase chain reaction (PCR), and wherein said amplification chamber contains: a preselected polynucleotide, a polymerase, nucleoside triphosphates, a first primer hybridizable with said sample polynucleotide, and a second primer hybridizable with a nucleic acid comprising a sequence complementary to said polynucleotide, wherein said first and second primers define the termini of the polynucleotide product of the polymerization reaction; and

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wherein said means for thermally cycling comprises means for thermally cycling the contents of said chamber between a temperature controlled to dehybridize double stranded polynucleotide thereby to produce single stranded polynucleotide, to permit annealing of said primers to complementary regions of single stranded polynucleotide, and to permit synthesis of polynucleotide between said primers, thereby to amplify said preselected polynucleotide.

95. The device of claim 93, wherein said solid substrate comprises microfabricated silicon.

96. A device for amplifying a preselected polynucleotide in a sample, the device comprising:

a solid substrate microfabricated to define;

a sample inlet port;

a flow system for micro- to picoliter volumes, comprising:

a sample flow channel extending  
from said inlet port; and  
  
a polynucleotide amplification  
reaction chamber, in fluid communication  
with said flow channel, containing a  
preselected polynucleotide and  
polynucleotide amplification reagents;  
  
said chamber and said channel being  
of dissimilar dimension; and  
  
a fluid exit port in fluid communication with  
said flow system; and  
  
means for thermally cycling the contents of said  
chamber whereby, in each cycle, temperature is  
controlled to dehybridize double stranded  
polynucleotide, and to permit synthesis of  
polynucleotide, thereby to amplify said preselected  
polynucleotide.

97. The device of claim 96, wherein said flow system  
further comprises a detection chamber in fluid communication with  
said amplification chamber.

98. A method for amplifying a preselected polynucleotide in  
a sample by conducting a polynucleotide amplification reaction,  
the method comprising:

- (i) providing a device comprising:  
a solid substrate microfabricated to define:

a sample inlet port;  
a flow system for micro- to picoliter volumes comprising:

a sample flow channel extending from said inlet port; and

a polynucleotide amplification reaction chamber in fluid communication with said flow channel;

said chamber and said channel being of dissimilar dimension; and

a fluid exit port in fluid communication with said flow system; and

means for thermally regulating the contents of said chamber at a temperature controlled to permit amplification of said preselected polynucleotide;

(ii) delivering, through said inlet port and said flow system to said reaction chamber, a sample polynucleotide and reagents required for an in vitro polynucleotide amplification reaction; and

(iii) thermally controlling the contents of said chamber to permit amplification of said polynucleotide.

99. The method of claim 98, wherein said amplification reaction is a polymerase chain reaction (PCR);

wherein in step (i), said means for thermally controlling comprises means for thermally cycling the contents of said chamber;

wherein step (ii) includes the step of adding to said amplification chamber: a polymerase, nucleoside triphosphates, a first primer hybridizable with said sample polynucleotide, and a second primer hybridizable with a nucleic acid comprising a sequence complementary to said polynucleotide, and wherein said first and second primers define the termini of the polynucleotide product of the polymerization reaction; and

wherein step (iii) includes the step of thermally cycling the contents of said chamber whereby, in each cycle, the temperature is controlled to dehybridize double stranded polynucleotide thereby to produce single stranded polynucleotide, to permit annealing of complementary regions of single stranded polynucleotide, and to permit synthesis and polymerization of polynucleotide between said primers.

100. A device for amplifying a preselected polynucleotide in a sample by conducting a polynucleotide amplification reaction, the device comprising:

a solid substrate microfabricated to define:  
a sample inlet port;  
a flow system for micro- to picoliter volumes, comprising:

a sample flow channel extending from  
said inlet port; and  
  
a polynucleotide amplification chamber,  
in fluid communication with said flow  
channel, said chamber containing reagents for  
amplifying a preselected polynucleotide in  
vitro;  
  
said chamber and said channel being of  
dissimilar dimension; and  
  
a fluid exit port in fluid communication  
with said flow system.

101. The device of claim 100, wherein said reagents comprise  
reagents for conducting a polymerase chain reaction.

102. A device for amplifying a preselected polynucleotide in  
a sample by conducting a polynucleotide amplification reaction,  
the device comprising:

a solid substrate which is microfabricated to  
define:

a sample inlet port;  
a flow system, comprising:

a sample flow channel extending from  
said inlet port; and  
a polynucleotide amplification reaction  
chamber in fluid communication with said flow  
channel;

said chamber and said channel being of dissimilar dimension; and

a fluid exit port in fluid communication with said flow system; and

means for thermally cycling the contents of said chamber whereby in each cycle the temperature is controlled to dehybridize double stranded polynucleotide and to permit the in-vitro amplification of a preselected polynucleotide.

103. The device of claim 102, wherein said amplification reaction is a polymerase chain reaction (PCR), and wherein said amplification chamber contains: a preselected polynucleotide, a polymerase, nucleoside triphosphates, a first primer hybridizable with said sample polynucleotide, and a second primer hybridizable with a nucleic acid comprising a sequence complementary to said polynucleotide, wherein said first and second primers define the termini of the polynucleotide product of the polymerization reaction; and

wherein said means for thermally cycling comprises means for thermally cycling the contents of said chamber between a temperature controlled to dehybridize double stranded polynucleotide thereby to produce single stranded polynucleotide, to permit annealing of said primers to complementary regions of single stranded polynucleotide, and to permit synthesis of polynucleotide between said primers, thereby to amplify said preselected polynucleotide.